L Number	Hits	Search Text	DB	Time stamp
-	9	"362711"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/25 08:35
-	18	Wolfe-henry.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 09:42
-	3	293557.ap.	USPAT	2003/08/15 09:45
-	4	118093.ap.	USPAT	2003/08/15 09:46
-	0	Hubbell-J$-.IN.	USPAT	2003/08/15 09:46
-	176	Hubbell.IN.	USPAT	2003/08/15 09:46
-	174582	1999.AY.	USPAT	2003/08/15 09:47
-	9	Hubbell.IN. AND 1999.AY.	USPAT	2003/08/15 09:50
-	0	WO-0002608-$.did.	USPAT	2003/08/15 09:51
-	8	Hubbell.IN. AND Elbert.in.	USPAT	2003/08/15 09:57
-	0	PCT/US00/02608.PCT	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 09:59
-	0	WO-0044808-$.did.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 09:59
-	1548015	WO 00/44808	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 10:12
-	164	(WO 00/44808) AND Hubbell.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 10:13
-	19	((WO 00/44808) AND Hubbell.in.) AND Elbert.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/15 10:13
-	1	"6376470"	USPAT	2003/08/15 13:02
-	1	("5641758").PN.	USPAT	2003/08/22 10:09
-	608	greenwald.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/25 08:35
-	370	514/49.ccls.	USPAT	2004/03/02 08:08
-	542	514/616.ccls.	USPAT	2004/03/02 08:08
-	286	536/28.5.ccls.	USPAT	2004/03/02 08:08
-	266	424/9.4.ccls.	USPAT	2004/03/02 08:08
-	261	424/78.17.ccls.	USPAT	2004/03/02 08:08
-	1055	564/152-153.ccls.	USPAT	2004/03/02 08:09
-	427	564/159.ccls.	USPAT	2004/03/02 08:09
-	120	greenwald-richard-b.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 08:09

-	2	"6395266"	USPAT	2004/03/02 08:16
-	6	"6395266"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 08:53
-	51	polymeric ADJ prodrug	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 08:53
-	2	polymeric ADJ prodrug AND 514/8.ccls.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 08:57
-	2144	514/8.ccls.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 08:57
-	23	514/8.ccls. AND ((polymeric WITH conjugate) OR polymeric ADJ prodrug)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 09:04
-	4	424/78.3.ccls. AND ((polymeric WITH conjugate) OR polymeric ADJ prodrug)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/03/02 09:04

HYDROXYPROPYLMETHACRYLAMIDE COPOLYMERS I. SUPPRESSION OF THE ANTIBODY
RESPONSE AND PROLIFERATION OF MOUSE SPLENOCYTES IN-VITRO.

=> d his

(FILE 'HOME' ENTERED AT 09:14:24 ON 02 MAR 2004)

INDEX 'BIOSIS, CAOLD, CAPLUS, CASREACT, CROPU, DGENE, DPCI, ENCOMPPAT2,
EUROPATFULL, FSTA, IFIPAT, INPADOC, JAPIO, NTIS, PAPERCHEM2, PATDD,
PATDPA, PATDPAFULL, PATOSDE, PATOSEP, PATOSWO, PCTFULL, PCTGEN, PIRA,
RAPRA, RDISCLOSURE, SYNTHLINE, TULSA, TULSA2, ...' ENTERED AT 09:15:44 ON
02 MAR 2004

SEA	PRODRUG
7766	FILE BIOSIS
1	FILE CAOLD
11399	FILE CAPLUS
556	FILE CASREACT
4	FILE CROPU
6358	FILE DGENE
595	FILE DPCI
1	FILE ENCOMPPAT2
2774	FILE EUROPATFULL
1	FILE FSTA
4436	FILE IFIPAT
5343	FILE INPADOC
271	FILE JAPIO
71	FILE NTIS
1	FILE PAPERCHEM2
8	FILE PATDD
206	FILE PATDPA
710	FILE PATDPAFULL
23	FILE PATOSDE
1363	FILE PATOSEP
1609	FILE PATOSWO
11563	FILE PCTFULL
53	FILE RAPRA
6	FILE RDISCLOSURE
127	FILE SYNTHLINE
14441	FILE USPATFULL

1312 FILE USPAT2
4671 FILE WPIDS
4671 FILE WPINDEX

L1 QUE PRODRUG

FILE 'BIOSIS' ENTERED AT 09:16:43 ON 02 MAR 2004

L2 371127 S PRODRUG OR POLYMER? OR CONJUGAT?
L3 3241 S POLYMER? AND CONJUGAT?
L4 251 S L3 AND DRUG DELIVER?
L5 22 S L4 AND PRODRUG
L6 142374 S (CONTROL? OR SLOW OR TIME? OR SUSTAIN?) (L) (RELEAS?)
L7 59 S L4 AND L6
L8 9 S L5 AND L6

=>

---Logging off of STN---

L8 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:205324 BIOSIS
DOCUMENT NUMBER: PREV200300205324
TITLE: Controlled release of proteins from their poly(ethylene glycol) conjugates: Drug delivery systems employing 1,6-elimination.
AUTHOR(S): Greenwald, Richard B. [Reprint Author]; Yang, Karen; Zhao, Hong; Conover, Charles D.; Lee, Stanford; Filpula, David
CORPORATE SOURCE: Enzon Pharmaceuticals Inc, 20 Kingsbridge Road, Piscataway, NJ, 08854, USA
richard.greenwald@enzon.com
SOURCE: Bioconjugate Chemistry, (March-April 2003) Vol. 14, No. 2, pp. 395-403. print.
ISSN: 1043-1802 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 2003
Last Updated on STN: 23 Apr 2003
AB Several tripartate releasable PEG linkers (rPEG) that can provide anchimeric assistance to hydrolysis (cyclization prodrugs) were prepared and, after conjugation to lysozyme demonstrated rapid cleavage in rat plasma compared to nonassisted, permanently bound PEG. By varying the chemical structure and adding steric hindrance, the half-life of the protein conjugates can be adjusted from slow to very fast. The pharmacokinetics (PK) of regeneration of native protein, from various rPEG conjugates can, for the first time, be easily followed in the rat using green fluorescent protein. The PK in mice was also determined for rPEG-Interleukin 2 (rPEG-IL-2) conjugates in vivo using an ELISA assay. Thus, a systematic study of rPEGylated proteins, either in vivo or in vitro during processing, has been investigated based on regeneration of native protein. The employment of releasable PEG polymers substantially broadens the applications of PEGylation drug delivery technology by introducing the benefits of controlled release of native protein therapeutics.
TI Controlled release of proteins from their poly(ethylene glycol) conjugates: Drug delivery systems employing 1,6-elimination.

L8 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:238827 BIOSIS

DOCUMENT NUMBER: PREV200200238827
TITLE: The use of polysaccharides to target drugs to the colon.
AUTHOR(S): Vandamme, Th. F. [Reprint author]; Lenourry, A.; Charrueau, C.; Chaumeil, J.-C.
CORPORATE SOURCE: Laboratoire de chimie therapeutique et nutritionnelle: Biodisponibilite tissulaire, Faculte de Pharmacie, Universite Louis Pasteur, Strasbourg, France
vandamme@pharma.u-strasbg.fr
SOURCE: Carbohydrate Polymers, (15 May, 2002) Vol. 48, No. 3, pp. 219-231. print.
CODEN: CAPOD8. ISSN: 0144-8617.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002
AB Targeting pharmaceutical drugs to the colon makes it possible to guarantee local or systemic drug delivery to this site. To deliver the compounds in a non-degraded form to the last part of the gastrointestinal tract, they must first of all pass through the stomach, the upper part of the intestine and must use the characteristics of the colon to specifically release the drugs in this part of the digestive tract. Usual methods for the specific delivery of drugs to the colon are based on the chemical or technological modification of excipients. Among these, pH-dependent coatings or those degraded specifically by the colonic microflora make it possible to create dosage forms containing high levels of drugs compared to matrix or hydrogel systems. Nevertheless, inter- and intra-individual variations in gut pH and in transit time along the gastrointestinal tract can stand in the way of specific drug delivery. To improve the specificity of drug release, certain types of polysaccharides can be used to create the dosage forms. These excipients are specifically degraded by the colonic microflora and have been used as polymer drug conjugates, coatings and matrix agents. However, most of these compounds are strongly hydrophilic leading to premature release. For these reasons, some polysaccharides, such as inulin, amylose, guar gum and pectins, have been chemically modified to increase their hydrophobicity or have been combined with other conventional hydrophobic polymers. This article reviews the potential uses of polysaccharides, the limits and the future developments in this field with these natural polymers.
TI The use of polysaccharides to target drugs to the colon.

L8 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:474364 BIOSIS

DOCUMENT NUMBER: PREV200000474364
TITLE: Labile conjugation of a hydrophilic drug to PLA oligomers to modify a drug delivery system: Cephradin in a PLAGA matrix.
AUTHOR(S): Ustariz-Peyret, C.; Coudane, J. [Reprint author]; Vert, M.; Kaltsatos, V.; Boisrame, B.
CORPORATE SOURCE: Faculty of Pharmacy, CRBA-UMR CNRS 1465, University Montpellier 1, 15, Ave. Charles Flahault, 34060, Montpellier, France
SOURCE: Journal of Microencapsulation, (September-October, 2000) Vol. 17, No. 5, pp. 615-624. print. CODEN: JOMIEF. ISSN: 0265-2048.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Nov 2000
Last Updated on STN: 10 Jan 2002
AB The physical entrapment of a hydrophilic drug within degradable microspheres is generally difficult because of poor entrapment yield and/or fast release, depending on the microsphere fabrication method. In order to counter the effects of drug hydrophilicity, it is proposed to covalently attach the drug to lactic acid oligomers, with the aim of achieving temporary hydrophobization and slower release controlled by the separation of the drug from the degradable link within the polymer matrix. This strategy was tested on microspheres of the antibiotic cephradin. As the prodrug form, the entrapment of the drug was almost quantitative. The prodrug did degrade in an aqueous medium, modelling body fluids, but cleavage did not occur at the drug-oligomer junction and drug molecules bearing two lactyl residual units were released. When the prodrug is entrapped within a PLAGA matrix, no release was observed within the experimental time period. However, data suggest that conjugation via a bond more sensitive to hydrolysis than the main chain PLA ester bonds should make the system work as desired.
TI Labile conjugation of a hydrophilic drug to PLA oligomers to modify a drug delivery system: Cephradin in a PLAGA matrix.

L8 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:430626 BIOSIS
DOCUMENT NUMBER: PREV199900430626
TITLE: High-molecular weight HPMA copolymer-adriamycin conjugates.
AUTHOR(S): Dvorak, M.; Kopeckova, P.; Kopecek, J. [Reprint author]
CORPORATE SOURCE: Departments of Pharmaceutics and Pharmaceutical Chemistry/CCCD, and of Bioengineering, University of Utah,

Salt Lake City, UT, 84112, USA
SOURCE: Journal of Controlled Release, (Aug. 5, 1999) Vol. 60, No. 2-3, pp. 321-332. print.
CODEN: JCREEC. ISSN: 0168-3659.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999
AB High-molecular weight (branched) water-soluble N-(2-hydroxypropyl)methacrylamide (HPMA) copolymers containing lysosomally degradable oligopeptide crosslinks were synthesized by radical copolymerization of HPMA and newly designed crosslinking agents, N2,N5-bis(N-methacryloylglycylphenylalanylleucylglycyl)ornithines with different modification of the carboxy group. The length of the primary chain was controlled by the addition of a chain transfer agent, 3-mercaptopropionic acid. A polymerizable derivative of the anticancer drug adriamycin (ADR), N-methacryloylglycylphenylalanylleucylglycyl adriamycin, was added to some polymerization mixtures. This resulted in high-molecular weight, branched, water-soluble HPMA copolymers containing oligopeptide sequences in the crosslinks as well as in side-chains terminated in ADR. The degradability of the crosslinks as well as the release of ADR by lysosomal enzymes isolated from rat liver were investigated.
TI High-molecular weight HPMA copolymer-adriamycin conjugates.

L8 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:121938 BIOSIS
DOCUMENT NUMBER: PREV199799428441
TITLE: Polymeric drug delivery of enzymatically degradable pendant agents: Peptidyl-linked procainamide model system studies.
AUTHOR(S): Sintov, Amnon [Reprint author]; Levy, Robert J.
CORPORATE SOURCE: Ben-Gurion Univ. Negev, Inst. Applied Res., Ernst David Bergmann Campus, PO Box 653, Beer-Sheva 84105, Israel
SOURCE: International Journal of Pharmaceutics (Amsterdam), (1997) Vol. 146, No. 1, pp. 55-62.
CODEN: IJPHDE. ISSN: 0378-5173.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Mar 1997
Last Updated on STN: 25 Mar 1997
AB Biodegradable polymeric drug delivery systems have become increasingly important for sustained release indications when a time-limited drug implant is required. A new methacrylic copolymer consisting of enzymatically-

cleavable oligopeptidyl procainamide as pendant side chains was synthesized in a series of three reactions. Using high performance liquid chromatography (HPLC) analysis, procainamide release was monitored while incubating polymer specimens in the presence of a model enzyme, alpha-chymotrypsin, in a physiologic buffer at 37 degree C. It was found that the new polymeric drug conjugate was insoluble in aqueous solutions and it was relatively stable when not in the presence of the enzyme, releasing not more than 5 mg of drug/g polymer after 30 days incubation under physiologic conditions. However, in the presence of alpha-chymotrypsin, the procainamide side chains were gradually enzymatically cleaved over 20 days, and the rate of hydrolysis could be controlled by varying the enzymatic incubation conditions. The enzymatic rate dependency of each formulation was dependent upon the comonomer ratio and the degree of crosslinking. These two factors influenced the accessibility of the water-insoluble polymers to enzyme. It is concluded that procainamide release from an enzymatically degradable pendant-peptide link can be achieved in an enzymatically controllable manner.

TI Polymeric drug delivery of enzymatically degradable pendant agents: Peptidyl-linked procainamide model system studies.

L8 ANSWER 6 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1996:338113 BIOSIS

DOCUMENT NUMBER: PREV199699060469

TITLE: Macromolecular prodrugs. VII. Polymer -dopamine conjugates.

AUTHOR(S): Kalcic, I.; Zorc, B. [Reprint author]; Butula, I.

CORPORATE SOURCE: Fac. Pharm. Biochem., Univ. Zagreb, HR-10000 Zagreb, Croatia

SOURCE: International Journal of Pharmaceutics (Amsterdam), (1996) Vol. 136, No. 1-2, pp. 31-36.
CODEN: IJPHDE. ISSN: 0378-5173.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Jul 1996
Last Updated on STN: 26 Sep 1996

AB Dopamine (3,4-dihydroxyphenetylamine, DOP) was covalently linked to poly(alpha,beta-(N-2-hydroxyethyl-DL-aspartamide)) (PHEA) and styrene-maleic anhydride copolymer (SMA) in order to prepare polymeric prodrugs as a potentially more stable form of dopamine. Release of active substance from polymer drug conjugates was studied in different buffer solutions at 37 +- 0.1 degree C. The following rate constants for PHEA-DOP were obtained:

k = 2.50 x 10-2 min-1 (pH = 1.2); k = 4.09 times 10-3 min-1 (pH = 7.4), and k = 1.71 times 10-2 min-1 (pH = 9.2). The rate constants for SMA-DOP were: k = 2.27 times 10-3 min-1 (pH = 7.4) and k = 7.98 times 10-3 min-1 (pH = 9.2).

TI Macromolecular prodrugs. VII. Polymer-dopamine conjugates.

L8 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1996:230546 BIOSIS

DOCUMENT NUMBER: PREV199698794675

TITLE: Intratumoural distribution as a determinant of tumour responsiveness to therapy using polymer-based macromolecular prodrugs.

AUTHOR(S): Steyger, P. S. [Reprint author]; Baban, D. F.; Brereton, M.; Ulbrich, K.; Seymour, L. W.

CORPORATE SOURCE: R.S. Dow Neurol. Sci. Inst., 1120 N.W. 20th Ave., Portland, OR 97212, USA

SOURCE: Journal of Controlled Release, (1996) Vol. 39, No. 1, pp. 35-46.
CODEN: JCREEC. ISSN: 0168-3659.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 28 May 1996
Last Updated on STN: 28 May 1996

AB Certain solid tumours (e.g., P388 murine leukaemia) regress completely when treated with soluble polymer-based prodrugs such as doxorubicin-N-(2-hydroxypropyl) methacrylamide (HPMA) copolymer conjugates, while others (e.g., B16F10 murine melanoma, LS174T human colorectal carcinoma xenografts) show only transient growth inhibition (Duncan et al., J. Control. Release, 19 (1992) 331-346). Here we have examined physiological factors potentially influencing responsiveness to such macromolecular prodrugs. Tumour uptake of drug probably contributes to response and a radiolabelled HPMA copolymer probe (297 kDa) showed passive accumulation up to 6.6%/g (P388), 10.4%/g (B16F10) and 6.1%/g (LS174T) after 24-48 h. Vascular permeability is thought to influence passive targeting, although levels of mRNA encoding the permeability-controlling vascular endothelial growth factor (VEGF) were similar in P388 and B16F10 tumours. Epifluorescence microscopy using FITC-dextran (70 kDa) showed macromolecular extravasation within all tumours, with accumulation at the periphery of B 16F10 and LS 174T and throughout the interstitium of P388 tumours. The greater chemosensitivity to doxorubicin of P388 cells (IC-50 120 nM) compared with B16F10 (688 nM) and LS 174T (723 nM) probably contributes to responsiveness, although the amount of prodrug reaching the tumour may be less important than its localisation, resulting

from the distribution of hyperpermeable tumour vasculature.
TI Intratumoural distribution as a determinant of tumour responsiveness to therapy using polymer-based macromolecular prodrugs.

L8 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1990:50919 BIOSIS
DOCUMENT NUMBER: PREV199089028283; BA89:28283
TITLE: DELIVERY OF ANTICANCER DRUGS.
AUTHOR(S): ZEE-CHENG R K-Y [Reprint author]; CHENG C C
CORPORATE SOURCE: DEP PHARMACOL TOXICOL THERAP, UNIV KANSAS CANCER CENT,
KANSAS CITY, KANSAS 66103, USA
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (1989) Vol. 11, No. 7-8, pp. 439-529.
CODEN: MFEPDX. ISSN: 0379-0355.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Jan 1990
Last Updated on STN: 27 Feb 1990
AB Chemotherapy is a major therapeutic approach for the treatment of both localized and metastasized cancers. Since anticancer drugs are neither specific nor targeted to the cancer cells, improved delivery of anticancer drugs to tumor tissues in humans appears to be a reasonable and achievable challenge. Scientists are working to increase the availability of drug for tumor uptake by 1) delaying the release preparations for long- lasting actions; 2) using liposome-entrapped drugs for prolonged effect or reduced toxicity; 3) administrating inert, non-toxic prodrugs for specific activations at the tumor site; 4) delivering the antibody-mediated drugs; 5) conjugating site-specific carriers to direct the drug to the tumor target. The latter depends heavily on pharmacokinetic investigations. Some success has been achieved in enhancing the efficacy and reducing the toxicity of drugs. Pharmacokinetic and pharmacodynamic considerations are two areas which have been focused toward the quantitative pharmacological studies of anticancer drugs in this manuscript. This review covers biodistribution and elimination, furnishing information on body clearance and unveiling sites of major metabolism; administration of anticancer drugs via various routes for optimal utilization: intra-arterial infusion for localized tumors, intrahecal, intraperitoneal and intrapleural injection for regional cavity administration. Conventional delivery routes, doses, pharmacokinetics data and elimination routes of therapeutic anticancer drugs are tabled. General approaches for delivery of anticancer drugs in achieving therapeutic improvements are outlined and correlated. Mechanism of drug resistance, and specific changes affecting the delivery of

available chemotherapeutic agents, as well as the drugs to restore the sensitivities to agents of resistant tumor cells, are discussed. This monograph covers the developments and progress in the delivery of anticancer drugs in two approaches: the theoretical approach, including pharmacokinetic and pharmacodynamic considerations, therapeutic implications and mechanism of drug resistance, and the practical approach, including the physical, chemical, biochemical and physiological considerations. Among these, physical approach for the delivery of anticancer agents to target sites (via microparticulate drug carriers: nanoparticles, liposomes, microspheres and activated carbon as well as the magnetic microcapsules) has shown recognizable improvements in prolonging anticancer effects and reducing toxicities. Implantable pumps and reservoirs for regional chemotherapy provide external control of delivery rate. The implanted systems, in general, yield better results than the traditional treatments in the treatment of liver and brain cancer. Chemical approaches for the improvements of drug delivery use prodrugs, biodegradable polymers and macromolecular matrix techniques. Modification of drug structure aims for better delivery through the action of prodrugs to improve their stability, solubility, tissue penetration properties and drug distribution, and to overcome resistance and alter the pharmacokinetic nature and selective activation at the target cells. The prodrug approach has definitely produced outstanding results in preserving stability, prolonging activity, reducing toxicity of parent drugs, and hopefully, producing active forms at targeted sites. Biodegradable polymers have demonstrated their increasing importance in practical applications. The macromolecular matrices approach and the biochemical approach for antibody-mediated drug delivery , although of theoretical interests, are still in the investigational stage. More practical and elegant preparations of components and conjugation to the drug system should be sought so that sufficient amounts of the delivery systems could be accumulated for the evaluation and comparison in humans. Promising results would then change the strategic mirage to a stratagemic miracle to achieve an ideal delivery system of anticancer drugs. A thorough understanding of the phy.

TI DELIVERY OF ANTICANCER DRUGS.

L8 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1989:361574 BIOSIS

DOCUMENT NUMBER: PREV198988053688; BA88:53688

TITLE: ACTION OF POLYMERIC PRODRUGS BASED ON N-2 HYDROXYPROPYLMETHACRYLAMIDE COPOLYMERS I. SUPPRESSION OF THE ANTIBODY RESPONSE AND PROLIFERATION OF MOUSE SPLENOCYTES IN-VITRO.

AUTHOR(S): RIHOVA B [Reprint author]; VETVICKA V; STROHALM J; ULBRICH
K; KOPECEK J
CORPORATE SOURCE: INST MICROBIOL, VIDENSKA 1083, 142 20 PRAGUE 4, CZECHOSLOVAKIA
SOURCE: Journal of Controlled Release, (1989) Vol. 9, No. 1, pp. 21-32.
CODEN: JCREEC. ISSN: 0168-3659.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 2 Aug 1989
Last Updated on STN: 23 Sep 1989
AB Splenocytes were removed from A/J mice 14 days after i.p. injection of 1 . times. 108 sheep red blood cells and were incubated for 10 min, 3 h and 5 days with free daunomycin, free anti Thy 1.2 antibodies or daunomycin conjugated to N-(2-hydroxypropyl)metharcrylamide (HPMA) copolymer conjugates with biodegradable (Gly-Leu-Gly; Gly-Phe-Leu-Gly) or non-biodegradable (Gly-Gly) side-chains containing targeting anti Thy 1.2 antibodies. The effect on the antibody response, represented by decrease in the numbers of IgM and IgG plaque-forming, i.e., antibody-releasing mouse splenocytes (plaque-forming cells), was detected. It was shown that a 10 min contact of immunocompetent cells with daunomycin-HPMA copolymer conjugates is sufficient for suppression of antibody formation. However, 3 hours incubation were necessary to obtain significant decrease in a number of PFC. Lymphocytes (mouse splenocytes) were very sensitive to free daunomycin. Concentration of 50 <SYM109>g/ml eliminated all lymphocytes from tissue culture. At 1-10 <SYM109>g/ml, a high proportion of cells remained viable, but the antibody response was completely suppressed. A comparable amount of daunomycin (35-70 <SYM109>g/ml) bound to copolymer with targeting antibodies did not kill lymphocytes in tissue culture, but the antibody response was substantially suppressed (50-90%). In all experiments IgG antibody formation was more sensitive to suppression than IgM response. Biodegradability of the bond between the HPMA copolymer carrier and daunomycin substantially increased the pharmacological effect although a certain degree of immunosuppression was detected with the drug conjugated to targeted non-biodegradable HPMA copolymer. Free daunomycin inhibited [3H]thymidine incorporation by mouse T lymphocytes (cultivation in presence of Con A) at the concentration of 0.1 <SYM109>g/ml. To achieve the same effect, 5 times more daunomycin bound to biodegradable HPMA copolymer with targeting anti Thy 1.2 antibodies or 500 times more daunomycin bound to non-targeted biodegradable HPMA copolymer was necessary.
TI ACTION OF POLYMERIC PRODRUGS BASED ON N-2